

In re Application of:  
Pan et al.  
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**Amendments to the Claims**

Please amend claims 5, 22, 25-27, 43 and 63-64 as indicated in the listing of claims.

Please cancel claims 1-4, 15-17, 19-21, 38-42, 53-55 and 57-59 without prejudice as they are drawn to non-elected subject matter.

Please cancel claims 13-14, 23-24, 28-29, 36, 51-52, 60-62 without prejudice.

The listing of claims will replace all prior versions, and listings of claims in the application.

**Listing of Claims:**

1.- 4. (Canceled).

5. (Currently amended) A modified IL-4 mutein receptor antagonist wherein the amino acid residue at position 37, 38, or 104 is cysteine and produced by the method of claim 4,

a) culturing a host cell comprising an expression vector comprising a polynucleotide sequence as set forth in SEQ ID NO: 4, SEQ ID NO: 5, or SEQ ID NO: 6; and

b) purifying the antagonist from the host cell culture,  
wherein the antagonist inhibits IL-4 and IL-13-mediated activity.

6. (Original) The modified IL-4 mutein receptor antagonist of claim 5 coupled to a non-protein polymer selected from the group consisting of polyethylene glycol, polypropylene glycol and polyoxyalkylenes.

7. (Original) The modified IL-4 mutein receptor antagonist of claim 6 wherein the modified mutein receptor antagonist binds to the IL-4 receptor alpha chain with a  $K_d$  of

about 0.1 nM to about 10  $\mu$ M, about 0.5 nM to about 1  $\mu$ M, or about 1.0 nM to about 100 nM.

8. (Original) The modified IL-4 mutein receptor antagonist of claim 6 wherein the modified IL-4 mutein receptor antagonist inhibits the proliferative response of TF-1 cells to IL-4 with an  $IC_{50}$  of about 0.1 nM to about 10  $\mu$ M, about 0.5 nM to about 1  $\mu$ M, or about 1.0 nM to about 100 nM.

9. (Original) The modified IL-4 mutein receptor antagonist of claim 6 wherein the modified IL-4 mutein receptor antagonist inhibits the proliferative response of TF-1 cells to IL-13 with an  $IC_{50}$  of about 0.1 nM to about 10  $\mu$ M, about 0.5 nM to about 1  $\mu$ M, or about 1.0 nM to about 100 nM.

10. (Original) The modified IL-4 mutein receptor antagonist of claim 6 wherein the modified IL-4 mutein receptor antagonist inhibits the proliferative response of human B cells to IL-4 with an  $IC_{50}$  of about 0.1 nM to about 10  $\mu$ M, about 0.5 nM to about 1  $\mu$ M, or about 1.0 nM to about 100 nM.

11. (Original) The modified IL-4 mutein receptor antagonist of claim 6 wherein the modified IL-4 mutein receptor antagonist inhibits the proliferative response of human T cells to IL-4 with an  $IC_{50}$  of about 0.1 nM to about 10  $\mu$ M, about 0.5 nM to about 1  $\mu$ M, or about 1.0 nM to about 100 nM.

12. (Original) The modified IL-4 mutein receptor antagonist of claim 6 wherein the modified IL-4 mutein receptor antagonist has a plasma half-life which is at least about 2-10 fold greater than that of an unmodified IL-4 receptor antagonist.

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13.-14. (Canceled).

15.-17. (Canceled).

18. (Original) A pharmaceutical composition comprising:

- a) the modified IL-4 mutein receptor antagonist of claim 6; and
- b) a pharmaceutically acceptable carrier.

19.-21. (Canceled).

22. (Currently amended) A modified IL-4 mutein receptor antagonist coupled to a non-protein polymer at an ~~[[amino]]~~ amino acid residue at position ~~28, 36, 37, 38, or 104, 105 or 106~~ of IL-4, wherein the amino acid at 37, 38 or 104 is cysteine, and wherein the non-protein polymer is polyethylene glycol, polypropylene glycol or a polyoxyalkylene.

23.-24. (Canceled)

25. (Currently amended) The modified IL-4 mutein receptor antagonist of claim 6 or 22 comprising an amino acid sequence as set forth in SEQ ED NO: 12.

26. (Currently amended) The modified IL-4 mutein receptor antagonist of claim 6 or 22 comprising an amino acid sequence as set forth in SEQ ID NO: 13.

27. (Currently amended) The modified IL-4 mutein receptor antagonist pf claim 6 or 22 comprising an amino acid sequence as set forth in SEQ ID NO: 14.

28.-29. (Canceled).

30. (Original) The modified IL-4 mutein receptor antagonist of claim 22 wherein the modified mutein receptor antagonist binds to the IL-4 receptor alpha chain with a  $K_d$  of about 0.1 nM to about 10  $\mu$ M, about 0.5 nM to about 1  $\mu$ M, or about 1.0 nM to about 100 nM.

31. (Original) The modified IL-4 mutein receptor antagonist of claim 22 wherein the modified IL-4 mutein receptor antagonist inhibits the proliferative response of TF-1 cells to IL-4 with an  $IC_{50}$  of about 0.1 nM to about 10  $\mu$ M, about 0.5 nM to about 1  $\mu$ M, or about 1.0 nM to about 100 nM.

32. (Original) The modified IL-4 mutein receptor antagonist of claim 22 wherein the modified IL-4 mutein receptor antagonist inhibits the proliferative response of TF-1 cells to IL-13 with an  $IC_{50}$  of about 0.1 nM to about 10  $\mu$ M, about 0.5 nM to about 1  $\mu$ M, or about 1.0 nM to about 100 nM.

33. (Original) The modified IL-4 mutein receptor antagonist of claim 22 wherein the modified IL-4 mutein receptor antagonist inhibits the proliferative response of human B cells to IL-4 with an  $IC_{50}$  of about 0.1 nM to about 10  $\mu$ M, about 0.5 nM to about 1  $\mu$ M, or about 1.0 nM to about 100 nM.

34. (Original) The modified IL-4 mutein receptor antagonist of claim 22 wherein the modified IL-4 mutein receptor antagonist inhibits the proliferative response of human T

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cells to IL-4 with an  $IC_{50}$  of about 0.1 nM to about 10  $\mu$ M, about 0.5 nM to about 1  $\mu$ M, or about 1.0 nM to about 100 nM.

35. (Original) The modified IL-4 mutein receptor antagonist of claim 22 wherein the modified IL-4 mutein receptor antagonist has a plasma half-life which is at least about 2-10 fold greater than that of an unmodified IL-4 receptor antagonist.

36. (Canceled).

37. (Original) A pharmaceutical composition comprising:

- a) the modified IL-4 mutein receptor antagonist of claim 22; and
- b) a pharmaceutically acceptable carrier.

38.-42. (Canceled).

43. (Currently amended) A modified IL-4 mutein receptor antagonist wherein the amino acid at 37, 38 and 104 is cysteine, and produced by the method of claims 41 or 42

a) culturing a host cell comprising an expression vector comprising a polynucleotide sequence as set forth in SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, wherein the antagonist is expressed;

b) allowing the antagonist to refold in the presence of dithiothreitol; and

c) purifying the antagonist from the host cell culture,

wherein the antagonist inhibits IL-4 and IL-13-mediated activity.

44. (Original) The modified IL-4 mutein receptor antagonist of claim 43 wherein the non-protein polymer is polyethylene glycol, polypropylene glycol or a polyoxyalkylene.

45. (Original) The modified IL-4 mutein receptor antagonist of claim 44 wherein the modified mutein receptor antagonist binds to the IL-4 receptor alpha chain with a  $K_d$  of about 0.1 nM to about 10  $\mu$ M, about 0.5 nM to about 1  $\mu$ M, or about 1.0 nM to about 100 nM.

46. (Original) The modified IL-4 mutein receptor antagonist of claim 44 wherein the modified IL-4 mutein receptor antagonist inhibits the proliferative response of TF-1 cells to IL-4 with an  $IC_{50}$  of about 0.1 nM to about 10  $\mu$ M, about 0.5 nM to about 1  $\mu$ M, or about 1.0 nM to about 100 nM.

47. (Original) The modified IL-4 mutein receptor antagonist of claim 44 wherein the modified IL-4 mutein receptor antagonist inhibits the proliferative response of TF-1 cells to IL-13 with an  $IC_{50}$  of about 0.1 nM to about 10  $\mu$ M, about 0.5 nM to about 1  $\mu$ M, or about 1.0 nM to about 100 nM.

48. (Original) The modified IL-4 mutein receptor antagonist of claim 44 wherein the modified IL-4 mutein receptor antagonist inhibits the proliferative response of human B cells to IL-4 with an  $IC_{50}$  of about 0.1 nM to about 10  $\mu$ M, about 0.5 nM to about 1  $\mu$ M, or about 1.0 nM to about 100 nM.

49. (Original) The modified IL-4 mutein receptor antagonist of claim 44 wherein the modified IL-4 mutein receptor antagonist inhibits the proliferative response of human T

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cells to IL-4 with an  $IC_{50}$  of about 0.1 nM to about 10  $\mu$ M, about 0.5 nM to about 1  $\mu$ M, or about 1.0 nM to about 100 nM.

50. (Original) The modified IL-4 mutein receptor antagonist of claim 44 wherein the modified IL-4 mutein receptor antagonist has a plasma half-life which is at least about 2-10 fold greater than that of an unmodified IL-4 receptor antagonist.

51.-52. (Canceled).

53.-55. (Canceled).

56. (Original) A pharmaceutical composition comprising:

- a) the modified IL-4 mutein receptor antagonist of claim 43; and
- b) a pharmaceutically acceptable carrier.

57.-59. (Canceled).

60.-62. (Canceled).

63. (Currently amended) A modified IL-4 mutein receptor antagonist of claim 43 ~~60 or 61~~, wherein the non-protein polymer is polyethylene glycol, polypropylene glycol or a polyoxyalkylene.

64. (Currently amended) The modified IL-4 mutein receptor antagonist of claim 43 ~~[[63]]~~, wherein the non-protein polymer is polyethylene glycol (PEG).